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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/779,957	02/09/2001	Kristi D. Snell	MBX 038	7578

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EXAMINER

BAUM, STUART F

ART UNIT	PAPER NUMBER
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1638

DATE MAILED: 04/09/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/779,957

Applicant(s)

SNELL, KRISTI D.

Examiner

Stuart F. Baum

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1,2,6-16,18 and 20-28 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,2,6-16,18 and 20-28 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 12 April 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_.
- 4) ☐ Interview Summary (PTO-413) Paper No(s) \_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

### **DETAILED ACTION**

1. The amendment entered 1/28/2003 has been entered.  
Claims 1, 2, 6-16, 18, and 20-28 are pending.  
Claims 3-5, 17 and 19 have been canceled.  
Claims 1, 11-12, 15-16, and 25-26 have been amended.
2. Claims 1, 2, 6-16, 18, and 20-28 are examined in the present office action.
3. The text of those sections of Title 35, U.S. Code not included in this office action can be found in a prior office action.

### ***Specification***

4. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See for example page 7, line 20. See MPEP § 608.01.

### ***Claim Objections***

5. Claims 12-14 are objected to for depending on a canceled claim. Correction is required.

### ***Enablement***

6. Claims 1-2, 6-16, 18, and 20-28 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make

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and/or use the invention. This rejection is maintained for the reasons of record set forth in the Official action mailed 10/23/2002. Applicant's arguments filed 1/28/2003 have been fully considered but they are not persuasive.

The Applicant contends that Example 1 clearly describes a construct for expressing two polypeptide encoding nucleic acids; GUS and GFP. The presence of the protein was detected using Western analysis. Applicants assert that the described procedure is not prophetic. Applicant critiques the literature cited by the Examiner that was used to demonstrate undue experimentation. In one instance, Applicant cites Perler (1998, Cell, 92:1-4) and explains that the reference is directed to "splicing" which is the result of combined activities that leads to ligation and production of a whole protein, starting from a polypeptide that included an intein separating two exteins. Applicant concludes by stating "through its raising of red flags in the overall protein splicing process, may shed light onto the process by which inteins are excised and the resulting exteins remain free of subsequent ligation" (page 6, end of main paragraph). Applicant contends that the procedures taught in Morassutti (2002, FEBS Letters 519:141-146) do not need to be addressed in specification because it is known in the art that extraneous reagents can cause chemical reactions when performed outside of their normal cellular location (page 7, 1<sup>st</sup> paragraph). Lastly, Applicant addresses Evans et al (2000, J. Biol. Chem. 275:9091-9094) and contend that the reference is directed to splicing, which is not what Applicant's invention is claiming. Applicants conclude by stating that "none of the Examiner's cited references cast any doubt onto the level of predictability of the claimed invention asserted by the applicant" and that splicing is not contemplated by the claims as pending (page 7, last paragraph and page 8, 2<sup>nd</sup> line).

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The Examiner concurs with the Applicant that the cited references deal with protein splicing and not with expressing multiple proteins from one construct. The claimed constructs and methods make use of inteins but in a modified capacity. There are many different types of inteins, as evidenced from the NEB web site, and there is more than one mechanism by which inteins accomplish their function (see for example Southworth et al., 2000, The Embo Journal 19(18):5019-5026). Because of the multiple pathways, it is not clear if all inteins can be modified to achieve the intentions of Applicant's broadly claimed invention. And because Applicant has claims drawn to all inteins, not just the specific one that is included in the Example, many of the parameters which are dealt with in the previously cited references as noted in the previous office action, are applicable because Applicant is modifying the original function of the claimed inteins. Because Applicant is using inteins for a purpose not normally found in nature, and because Applicants claims are drawn to all inteins, not just the one cited in Example 1, it would require undue experimentation by one skilled in the art to make and/or use the broadly claimed invention.

It should be noted, that Applicant stressed that Example 1 is not a prophetic description. The Examiner has re-read Example 1 and maintains that Example 1 is prophetic as no data is provided and it is written in a style that suggests what may be done, and not, what has been done. Why for instance, does Applicant detect the presence of GUS and GFP using Western analysis when a simple colorimetric analysis will suffice. GUS and GFP are reporter enzymes designed specifically for easy and immediate detection.

***Written Description***

7. Claims 1-2, 6-16, 18, and 20-28 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is maintained for the reasons of record set forth in the Official action mailed 10/23/2002. Applicant's arguments filed 1/28/2003 have been fully considered but they are not persuasive.

Applicant contends that the specification is replete with information disclosing inteins that are used in the claimed invention, and references locations in the specification which reference specific articles or a database which can be search for the pertinent information. The Applicant does not understand how the Examiner can assert that the invention is not described and then reject claims based on 102(b) art that teaches protein splicing was well known in the art at the time of filing the present application.

Applicant has not described the inteins that are utilized in the claimed subject matter. Applicant has merely referenced articles which deal with specific instances of intein modification. As has been stated in the argument above, Applicant is broadly claiming all inteins to be used in either a construct or method but the sequences of the claimed inteins have not been taught or disclosed in the specification. It is not enough to simply cite a reference that describes one instance of the claimed invention and to extrapolate the disclosed information to cover all intein sequences. Applicant has not described enough species to justify claiming a whole genus of inteins that are used in the claimed invention. In regards to Applicants not understanding how the Examiner can reject claims based on Written Description and then cite

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102(b) art against the claims; the Examiner is not contending that the process is not described, rather, the scope of the claims directed to all inteins is being rejected. Applicant has not described modifying all inteins so as to be useable in the claimed invention. As was stated previously, Applicant has not described the genus of inteins useable in the claimed invention.

***Prior Art***

8. Claims 1 and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Chong et al (The Journal of Biological Chemistry 271:22159-22168, list in IDS). This rejection is maintained for the reasons of record set forth in the Official action mailed 10/23/2002.

Applicant's arguments filed 1/28/2003 have been fully considered but they are not persuasive.

Applicant contends that the newly amended claims are not anticipated by the Chong et al reference because it fails to teach any construct or method that makes use of intein sequences that catalyze excision of exteins, wherein the excised exteins are not ligated.

The Examiner disagrees. Chong et al teach the construction of a construct comprising two exteins (maltose binding protein and thioredoxin ) and a yeast intein. Figure 5 teaches the excision of maltose binding protein and thioredoxin from a translated preprotein comprising the maltose binding protein, intein, and thioredoxin and as such, anticipates the claimed invention.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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9. Claims 1-2, 6-11, 15-16, 18, and 20-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 1 and 15, the metes and bounds of “modified” have not been defined. It is unclear how the intein sequence has been changed. In addition, it is unclear what is meant by “modified by fusing”. Does Applicant mean that the intein is modified because it is operably linked to the carboxy-terminus of a gene? How does the act of ligating a sequence to another “modify” the sequence?

In claims 1 and 15, Applicant recites “multiple genes or exteins” but does not specify an order. Is the order important to the proper functioning of the invention?

10. No claims are allowed.

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,



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however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart Baum whose telephone number is (703) 305-6997. The examiner can normally be reached on Monday-Friday 8:30AM – 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 or (703) 305-3014 for regular communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist, who may be contacted at 308-0196.

Stuart F. Baum Ph.D.

April 3, 2003

  
**ELIZABETH F. McELWAIN**  
**PRIMARY EXAMINER**  
**GROUP 1800**